

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) A method for diagnosing a bipolar disorder in a patient, comprising:
 - (a) obtaining a patient ratio of (i) the mean membrane potential of cells of the patient incubated in the absence of K⁺ to (ii) the mean membrane potential of cells of the patient incubated in the presence of K⁺; and one or both of the following steps (b) and (c):
 - (b) comparing the patient ratio obtained in (a) to a control ratio, wherein the control ratio is the ratio of (iii) the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the absence of K⁺ to (iv) the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the presence of K⁺, wherein a significant difference between the patient ratio compared to the control ratio indicates that the patient has said bipolar disorder;
 - (c) comparing the patient ratio obtained in (a) to a bipolar control ratio, wherein the bipolar control ratio is the ratio of (v) the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the absence of K⁺ to (vi) the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the presence of K⁺, wherein the lack of a significant difference between the patient ratio and the bipolar control ratio indicates that the patient has said bipolar disorder.

2. (original) The method according to claim 1, wherein steps (a) and (b) are performed.

3. (original) The method according to claim 1, wherein steps (a) and (c) are performed.

4. (original) The method according to claim 1, wherein steps (a), (b) and (c) are performed.

5. (original) The method according to claim 1, wherein when K⁺ is present, it is present at a concentration of 2 - 7 mM.

6. (original) The method according to claim 1, wherein the significant difference between the patient ratio compared to the control ratio is that the patient ratio is significantly higher than the control ratio.

7. (original) The method according to claim 1, wherein the cells of the patient are incubated in the presence of a compound that alters Na⁺K⁺ ATPase activity; and wherein the corresponding control cells, the corresponding bipolar control cells, or both the corresponding control cells and the corresponding bipolar control cells are also incubated in the presence of the compound that alters Na⁺K⁺ ATPase activity.

8. (original) The method according to claim 7, wherein the compound that alters Na⁺K⁺ ATPase activity is selected from the group consisting of: valinomycin, monensin, monensin decyl ester, gramicidin, *p*-chloromercurybenzenesulfonate (PCMBS), veratridine, ethacrynat, dopamine, a catecholamine, a phorbol ester, ouabain, lithium, valproate, lamotrigine, cocaine, nicotine, R0-31-8220, oxymetazoline, calcineurin, topiramate, a peptide hormone, sorbitol, and a diuretic.

9. (original) The method according to claim 7, wherein the compound that alters Na⁺K⁺ ATPase activity is a compound that increases Na⁺K⁺ ATPase activity.

10. (original) The method according to claim 7, wherein the compound that alters Na^+K^+ ATPase activity is ethacrynone.

11. (original) The method according to claim 10, wherein ethacrynone is present at a concentration of 1 - 100 μM .

12. (original) The method according to claim 7, wherein the compound that alters Na^+K^+ ATPase activity is monensin.

13. (original) The method according to claim 12, wherein monensin is present at a concentration of 1 - 50 μM .

14. (original) The method according to claim 7, wherein the compound that alters Na^+K^+ ATPase activity is a phorbol ester.

15. (original) The method according to claim 14, wherein the phorbol ester is selected from the group consisting of: phorbol 12-myristate 13-acetate (PMA), 12-O-tetradecanoylphorbol 13-acetate, phorbol 12-myristate 13-acetate 4-O-methyl ether, phorbol 12,13-dibutyrate (PDBu), phorbol 12,13-didecanoate (PDD), and phorbol 12,13-dinonanoate 20-homovanillate.

16. (original) The method according to claim 15, wherein the phorbol ester is phorbol 12-myristate 13-acetate (PMA).

17. (original) The method according to claim 16, wherein phorbol 12-myristate 13-acetate (PMA) is present at a concentration of 0.1 - 10 μM .

18. (original) The method according to claim 7, wherein the compound that alters Na^+K^+ ATPase activity is lithium.

19. (original) The method according to claim 18, wherein lithium is present at a concentration of 1 - 50 mM.

20. (original) The method according to claim 1, wherein the mean membrane potential of the cells of the patient is determined by incubating the cells of the patient with a voltage-sensitive fluorescent dye and measuring the fluorescence intensity of said fluorescent dye.

21. (original) The method according to claim 20, wherein the dye is a cell-permeant cationic dye.

22. (original) The method according to claim 20, wherein the dye is a carbocyanine dye.

23. (original) The method according to claim 20, wherein the dye is 3,3'-dihexyloxacarbocyanine iodide DiOC₆(3).

24. (original) The method according to claim 1, wherein the cells of the patient, the corresponding control cells, and the corresponding bipolar control cells are selected from the group consisting of: lymphoblasts, erythrocytes, platelets, leukocytes, macrophages, monocytes, dendritic cells, fibroblasts, epidermal cells, mucosal tissue cells, cells in the cerebrospinal fluid, hair cells, and cells in whole blood.

25. (original) The method according to claim 24, wherein the cells of the patient, the corresponding control cells, and the corresponding bipolar control cells are lymphoblasts.

26. (original) The method according to claim 24, wherein the cells of the patient, the corresponding control cells, and the corresponding bipolar control cells are cells in whole blood.

27. (currently amended) A method for diagnosing a bipolar disorder in a patient, comprising:

(a) obtaining a patient ratio of (i) the mean membrane potential of cells of the patient incubated in the presence of a compound that alters Na⁺K⁺ ATPase activity to (ii) the

mean membrane potential of cells of the patient incubated in the absence of the compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity; and one or both of the following steps (b) and (c):

(b) comparing the patient ratio obtained in (a) to a control ratio, wherein the control ratio is the ratio of (iii) the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the presence of a compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity to (iv) the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the absence of the compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity, wherein a significantly lower patient ratio compared to the control ratio indicates that the patient has said bipolar disorder;

(c) comparing the patient ratio obtained in (a) to a bipolar control ratio, wherein the bipolar control ratio is the ratio of (v) the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the presence of a compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity to (vi) the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the absence of the compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity, wherein the lack of a significant difference between the patient ratio compared to the bipolar control ratio indicates that the patient has said bipolar disorder.

28. (original) The method according to claim 27, wherein the cells are incubated in the presence of K^+ .

29. (original) The method according to claim 27, wherein the cells are incubated in the absence of K^+ .

30. (original) The method according to claim 27, wherein the cells incubated in the presence of the compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity are incubated in the absence

of K^+ , and wherein the cells incubated in the absence of the compound that alters Na^+K^+ ATPase activity are incubated in the presence of K^+ .

31. (original) The method according to claim 27, wherein the compound that alters Na^+K^+ ATPase activity is selected from the group consisting of: valinomycin, monensin, monensin decyl ester, gramicidin, *p*-chloromercurybenzenesulfonate (PCMBS), veratridine, ethacrynat, dopamine, a catecholamine, a phorbol ester, ouabain, lithium, valproate, lamotrigine, cocaine, nicotine, R0-31-8220, oxymetazoline, calcineurin, topiramate, a peptide hormone, sorbitol, and a diuretic.

32. (original) The method according to claim 31, wherein the compound that alters Na^+K^+ ATPase activity is ethacrynat.

33. (currently amended) A method for diagnosing a bipolar disorder in a patient, comprising:

(a) obtaining a ratio (patient ratio I) of (i) the mean membrane potential of cells of the patient incubated in the absence of K^+ and in the presence of a compound that alters Na^+K^+ ATPase activity to (ii) the mean membrane potential of cells of the patient incubated in the absence of K^+ and in the absence of the compound that alters Na^+K^+ ATPase activity;

(b) obtaining a ratio (patient ratio II) of (iii) the mean membrane potential of cells of the patient incubated in the presence of K^+ and in the presence of the compound that alters Na^+K^+ ATPase activity to (iv) the mean membrane potential of cells of the patient incubated in the presence of K^+ and in the absence of the compound that alters Na^+K^+ ATPase activity;

(c) obtaining a relative ratio (Relative Patient Ratio) of patient ratio I to patient ratio II; and one or both of the following steps (d) and (e):

(d) comparing the Relative Patient Ratio to a Relative Control Ratio, wherein the Relative Control Ratio is the relative ratio of control ratio I to control ratio II, wherein control

ratio I is the ratio of (i') the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the absence of K⁺ and in the presence of a compound that alters Na⁺K⁺ ATPase activity to (ii') the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the absence of K⁺ and in the absence of the compound that alters Na⁺K⁺ ATPase activity, and wherein control ratio II is the ratio of (iii') the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the presence of K⁺ and in the presence of the compound that alters Na⁺K⁺ ATPase activity to (iv') the mean membrane potential of corresponding control cells of one or more people known to not have said bipolar disorder incubated in the presence of K⁺ and in the absence of the compound that alters Na⁺K⁺ ATPase activity, wherein a significant difference between the Relative Patient Ratio compared to the Relative Control Ratio indicates that the patient has said bipolar disorder;

(e) comparing the Relative Patient Ratio to a Relative Bipolar Control Ratio, wherein the Relative Bipolar Control Ratio is the relative ratio of bipolar control ratio I to bipolar control ratio II, wherein bipolar control ratio I is the ratio of (i'') the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the absence of K⁺ and in the presence of a compound that alters Na⁺K⁺ ATPase activity to (ii'') the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the absence of K⁺ and in the absence of the compound that alters Na⁺K⁺ ATPase activity, and wherein bipolar control ratio II is the ratio of (iii'') the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the presence of K⁺ and in the presence of the compound that alters Na⁺K⁺ ATPase activity to (iv'') the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the presence of K⁺ and in the absence of the compound that alters Na⁺K⁺ ATPase activity, wherein a significant difference between the Relative Patient Ratio compared to the Relative Bipolar Control Ratio indicates that the patient has said bipolar disorder;

Na^+K^+ ATPase activity to (iv'') the mean membrane potential of corresponding bipolar control cells of one or more people known to have said bipolar disorder incubated in the presence of K^+ and in the absence of the compound that alters Na^+K^+ ATPase activity, wherein the lack of a significant difference between the Relative Patient Ratio compared to the Relative Bipolar Control Ratio indicates that the patient has said bipolar disorder.

34. (original) The method according to claim 33, wherein the compound that alters Na^+K^+ ATPase activity is selected from the group consisting of: valinomycin, monensin, monensin decyl ester, gramicidin, *p*-chloromercurybenzenesulfonate (PCMBS), veratridine, ethacrynat, dopamine, a catecholamine, a phorbol ester, ouabain, lithium, valproate, lamotrigine, cocaine, nicotine, R0-31-8220, oxymetazoline, calcineurin, topiramate, a peptide hormone, sorbitol, and a diuretic.

35. (currently amended) A method for diagnosing a bipolar disorder in a patient, comprising:

(a) ascertaining a mean rate of repolarization in cells of the patient incubated in the presence of a compound that alters Na^+K^+ ATPase activity; and one or both of the following steps (b) and (c):

(b) comparing the mean rate of repolarization ascertained in (a) to the mean rate of repolarization in corresponding control cells of one or more people known to not have said bipolar disorder incubated in the presence of the compound that alters Na^+K^+ ATPase activity, wherein a significant difference between the mean rate of repolarization in the cells of the patient compared to the mean rate of repolarization in the corresponding control cells indicates that the patient has said bipolar disorder;

(c) comparing the mean rate of repolarization ascertained in (a) to the mean rate of repolarization in corresponding bipolar control cells of one or more people known to have

said bipolar disorder incubated in the presence of the compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity, wherein the lack of a significant difference between the mean rate of repolarization in the cells of the patient compared to the mean rate of repolarization in the corresponding bipolar control cells indicates that the patient has said bipolar disorder.

36. (original) The method according to claim 35, wherein the cells are incubated in the presence of K^+ .

37. (original) The method according to claim 35, wherein the cells are incubated in the absence of K^+ .

38. (original) The method according to claim 35, wherein the compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity is selected from the group consisting of: valinomycin, monensin, monensin decyl ester, gramicidin, *p*-chloromercurybenzenesulfonate (PCMBS), veratridine, ethacrynone, dopamine, a catecholamine, a phorbol ester, ouabain, lithium, valproate, lamotrigine, cocaine, nicotine, R0-31-8220, oxymetazoline, calcineurin, topiramate, a peptide hormone, sorbitol, and a diuretic.

39. (original) A method for diagnosing unipolar disorder in a patient, comprising:
(a) obtaining a patient ratio of (i) the mean membrane potential of cells of the patient incubated in the presence of a compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity to (ii) the mean membrane potential of cells of the patient incubated in the absence of the compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity; and one or both of the following steps (b) and (c):

(b) comparing the patient ratio obtained in (a) to a control ratio, wherein the control ratio is the ratio of (iii) the mean membrane potential of corresponding control cells of one or more people known to not have unipolar disorder incubated in the presence of a compound that alters $\text{Na}^+ \text{K}^+$ ATPase activity to (iv) the mean membrane potential of corresponding control cells of one or more people known to not have unipolar disorder

incubated in the absence of the compound that alters Na^+K^+ ATPase activity, wherein a significantly higher patient ratio compared to the control ratio indicates that the patient has unipolar disorder;

(c) comparing the patient ratio obtained in (a) to a unipolar control ratio, wherein the unipolar control ratio is the ratio of (v) the mean membrane potential of corresponding unipolar control cells of one or more people known to have unipolar disorder incubated in the presence of a compound that alters Na^+K^+ ATPase activity to (vi) the mean membrane potential of corresponding unipolar control cells of one or more people known to have unipolar disorder incubated in the absence of the compound that alters Na^+K^+ ATPase activity, wherein the lack of a significant difference between the patient ratio compared to the unipolar control ratio indicates that the patient has unipolar disorder.

40. (original) The method according to claim 39, wherein the cells incubated in the presence of the compound that alters Na^+K^+ ATPase activity are incubated in the absence of K^+ , and wherein the cells incubated in the absence of the compound that alters Na^+K^+ ATPase activity are incubated in the presence of K^+ .

41. (original) The method according to claim 39, wherein the compound that alters Na^+K^+ ATPase activity is selected from the group consisting of: valinomycin, monensin, monensin decyl ester, gramicidin, *p*-chloromercurybenzenesulfonate (PCMBS), veratridine, ethacrynat, dopamine, a catecholamine, a phorbol ester, ouabain, lithium, valproate, lamotrigine, cocaine, nicotine, R0-31-8220, oxymetazoline, calcineurin, topiramate, a peptide hormone, sorbitol, and a diuretic.

42. (original) The method according to claim 41, wherein the compound that alters Na^+K^+ ATPase activity is ethacrynat.

43. (original) The method according to claim 39, wherein the cells of the patient, the corresponding control cells, and the corresponding unipolar control cells are cells in whole blood.

44. (new) The method of claim 1, wherein said bipolar disorder is bipolar I disorder.

45. (new) The method of claim 27, wherein said bipolar disorder is bipolar I disorder.

46. (new) The method of claim 33, wherein said bipolar disorder is bipolar I disorder.

47. (new) The method of claim 35, wherein said bipolar disorder is bipolar I disorder.